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# Medico-economic evaluation of infliximab in rheumatoid arthritis—prospective French study of a cohort of 635 patients monitored for two years

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**Objectives.** To perform, in real conditions of prescription, the medico-economic evaluation of infliximab in severe RA.
**Methods.** A cost–effectiveness analysis of the annual costs was done with a comparison between the previous and the following year under infliximab. The effectiveness, determined from the HAQ, was expressed in clinically significant units and in quality-adjusted life years (QALYs). The incremental net benefit (INB), defined as willingness to pay ($\lambda$), was used to express the results.
**Results.** A cohort of 635 patients was formed. Before the use of infliximab, after 1 and 2 years, the mean annual cost per patient for the care of RA was €9832, 27 723 and 46 704, respectively. Among the direct costs, infliximab accounts for €21 182 for the first year. The distribution of the different costs was similar after 2 years. By using the INB, the difference before and after 1 year under infliximab is significant, on average by 1.86 (S.E.M. = 0.76) when the effectiveness is expressed in clinically significant units. For severe HAQ, $\lambda$ is €9841 (18 593 for all HAQ). When it is expressed in QALYs, also for severe HAQ, $\lambda >$ €100 000. This can be explained by a short follow-up although severe complication of RA appears later.
**Conclusion.** An evaluation of the more long-term costs is required in order to determine whether there are any full economic benefits with this treatment.

**Key words:** Rheumatoid arthritis, Medico-economic, Infliximab, French cohort.

## Introduction

The prevalence of RA in France, the most common chronic inflammatory rheumatism, is between 0.31 and 0.40% of the population, that is 130 000–150 000 individuals (95 000–210 000) and its incidence ~20/100 000 [1,2]. About 30% or 39 000–45 000 patients suffer from the refractory forms to MTX. RA being the cause of major disability and alteration in quality of life has a high social and economic cost. After 10 years of evolution, almost half of the patients present a functional disability putting an end to all professional life [1,2]. The costs induced are difficult to measure since the clinical trials are generally too short to assess the economic impact of treatment. Infliximab, a TNF-$\alpha$ antagonist, therapeutic class that revolutionized the care of RA [3,4], obtained the marketing approval in Europe in 2000 for the treatment of severe RA. The high price raises the question of its financing by the public sector. In 2001, the French Health Department included infliximab in a programme for the support of expensive diagnostic and therapeutic innovations, which financed the treatment of 2000 patients with public funds. The French Society of Rheumatology was asked by it to co-ordinate the distribution of this exceptional funding between the rheumatology departments of university and general hospital centres according to their active file of patients with RA and to establish a study for the medico-economic evaluation of infliximab (EMER). The secondary goals of the study were to determine over 2 years, in clinical practice, the efficacy and tolerance of infliximab, conditions of its use and quality of life of the patients.

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## Patients and methods

### *Patients*

The EMER study is an observational, prospective and multicentric study having involved 74 rheumatology departments in university and general hospital centres. Of all the patients treated with infliximab (initially 3 mg/kg), we included one out of two patients in the study. A cohort of 635 patients was thereby formed and monitored for a period of 2 years after inclusion. The subject's written consent was obtained and the whole study was approved by the Regional Ethics Committee for Medical Research (Ethical Committee of Montpellier).

### *Efficacy criteria*

We evaluated pain using visual analogue scale (VAS), global VAS according to the doctor and the patient, disease activity score (DAS) 28 [tendency test carried out on patients with a DAS28 rating at each evaluation ($P < 0.0001$)], functional capacity with HAQ, quality of life using the Short Form 36 (SF-36), ESR and CRP.

### *Medico-economic data*

The analysis was carried out from the health insurance coverage point of view, that is, the institutional payer. The economic valorization was based on the direct (medical and non-medical) and indirect costs related to the treatment of RA. The intangible costs are not valorized as such but through their impact on the quality of life. The direct medical costs include hospitalization (administration of treatment and surgery), medical and technical procedures (consultations, physiotherapy, lab tests and X-rays), drug treatments and stays in convalescence homes or rehabilitation centres. The direct non-medical costs are represented by the transport (ambulance, non-emergency medical transport, private car, etc.), home care and equipment of the home (installation of railing, elevator, equipment of kitchen, etc.). The indirect costs are related to a loss of productivity for the society (work stoppage or disability of professionally active subjects) and include the

TABLE 1. Fees

| Type of cost | Nature of the cost | Reference fees | Fees at the time of the study |
|---|---|---|---|
| Direct medical costs | Hospitalization | National cost scale most adapted to the type of intervention | National ISA point: €2.11 |
| | Medico-technical procedures | General nomenclature fees for professional procedures | CS (consultation): €23<br>AMC (physiotherapy and ergotherapy): €1.98 |
| | | Rating from the key letter + coefficient of the procedures performed | B (lab tests): €0.27<br>Z (X-rays): €1.33 |
| | Drug treatments | 2003 prices for infliximab and drugs reserved for hospital use | Infliximab 2003[a]: €711 for one 100 mg bottle |
| | | Public price for drugs not reserved to hospital | |
| | Rest home | | €127.33 per day |
| | Rehabilitation centre | | €203.80 per day |
| Direct non-medical costs | Medicalized transport | National health rates (Languedoc-Roussillon region) | Private car: €0.26/km<br>Ambulance: €52 (trip <5 km) or €2/cm (trip >5 km)<br>Non-emergency medical transport: €0.78/km<br>N.B.: 100% reimbursement of expenses in disease with long-term disability |
| | Equipment and home care | | According to the information provided by the patient |
| Indirect costs | Work stoppages | According to the socioprofessional category | Employees and labourers: €63.30 per day |
| | Disabilities | INSEE scale for average annual net salaries of civil servants in 2000 | Intermediate professions: €74.90 per day<br>Managers: €110.30 per day |

[a]Price at the time of the study.

patients still working at the time of inclusion. All consumption of resources was noted by the patients (self-questionnaire). In order to compare the costs before and under infliximab, the patient was his own control and reported his consumption during the year prior to inclusion. The monetary valorization was based on the prevailing rates at the time of the analysis (2003; Table 1).

### *Statistical methodology*

The characteristics of the patients were described by the median (interquartile range) or by the mean ± S.D.; the HAQ and SF-36 scores were calculated according to the validated rules. An analysis in repeated measurements was carried out using Friedman's test and contrast analysis. The costs were described (mean, range) and compared between patients according to HAQ upon inclusion ($HAQ \leqslant 1$, $1 < HAQ \leqslant 1.5$ and $HAQ > 1.5$ groups) by using a Kruskal–Wallis test.

The marginal mean cost per patient was estimated using the method developed by Willan *et al*. [5] consisting of carrying out, at each interval separating two consecutive visits, linear regression models on the costs observed (validity of the regression models were checked on the non-censored data; results not shown). The marginal mean total cost was then estimated using the regression parameters. This method is adapted to our data since it can be used to introduce co-variates and take censored data into account. A cost–effectiveness analysis was then carried out. The effectiveness, estimated from the HAQ, was expressed in several ways:

- in clinically significant units with a variation of 0.25 points in the HAQ [6] for threshold value: a reduction of 1 point of HAQ represents a gain of four clinically significant units;
- in quality-adjusted life years (QALYs):
  - Based on Barton's regression model [7] (QALY = 0.862–0.327*HAQ) where a reduction of 1 point in the HAQ represents an increase of 0.327 QALY with 95% CI 0.29, 0.37 (a random effect was introduced in the change of HAQ in QALY from the standard error of the regression parameters of the Barton's model).
  - Based on the Birmingham Preliminary Model (BPM) where a reduction of 1 point of HAQ corresponds to an improvement of 0.20 QALY [8].

The incremental net benefit (INB) [9, 10] is an indicator equivalent to the cost–effectiveness ratio but easier to use. It is defined for a willingness to pay $\lambda$ by the formula $INB(\lambda) = \lambda \Delta E - \Delta C$ where $\Delta E$ is the difference in the mean of efficacy between the previous and first year under infliximab, and $\Delta C$ the difference in the mean of cost. $INB(\lambda) > 0$ means that, for the willingness to pay $\lambda$, the cost–effectiveness ratio is perhaps acceptable by the society and will be so if the 95% CI is positive and lower than the acceptable threshold $\lambda$ (€45 000 in France). The main analysis was performed using the definition of a clinically significant unit by Krishnan *et al*. [6] and the conversion of HAQ in QALYs using the Barton *et al*. [7] and the BPM [8] models.

## Results

Between November 2001 and April 2003, 635 patients (76% women) were included. Of the 74 participating centres, 21 (28%) recruited at least 10 patients. The leading five centres recruited 27% (169 patients) of the inclusions (Montpellier recruited 45 patients, Grenoble 35, Rouen 32, Nantes 29 and Strasbourg 28). The mean age at the first symptoms, diagnosis and inclusion (prescription of infliximab) were 40.9 ± 13.0, 42.3 ± 13.0 and 53.4 ±11.8 years, respectively. Seropositivity for the RF, tenosynovitis and rheumatoid nodules were noted in 86, 36 and 22% of the patients, respectively (Table 2). The median DAS28 is 5.82 (5.15–6.56) and 87% of the patients presented radiographic erosions, attesting to active and severe RA. Over 90% of the patients were treated with at least one NSAID and 98.7% with MTX.

Upon inclusion, the median VAS for pain was at 59 (43–70) and quickly decreased as of the second week of treatment, to 40 (25–53). After 1 year and, globally, 2 years of treatment, the median VAS decreased by 49% ($P < 0.0001$) and 58%, respectively. The median global VAS according to the patient decreases by 59% and globally by 62% ($P < 0.0001$), respectively. The scores provided by the doctors followed the same evolution (56 and 63% reduction, respectively). The initial median DAS28 (Fig. 1A) of the completers was 5.65 and decreased to 4.2 after 2 weeks. After the first and second years, the reduction continued with a score of 3.46 and 3.36, respectively. The initial median HAQ (Fig. 1B) of the completers was 1.63. After the first and second years, the reduction continued with a score of 1. Upon inclusion, all of the items comprising the SF-36 score were altered and improved perceptibly as of the third perfusion and stabilized during the 2-year period.

The treatment was prematurely interrupted by 391 patients. Causes were inefficacy (17% of all patients treated), serious (10%) or non-serious adverse effect (6%) and patient's wish (7%).

TABLE 2. Characteristics of the patients

| Parameter | *n* | Value |
|---|---|---|
| Number of swollen joints, median (IQR) | 630 | 9 (5–13) |
| Number of painful joints, median (IQR) | 624 | 12 (7–17) |
| Morning stiffness, median (IQR), min | 629 | 90 (45–120) |
| Pain VAS, median (IQR) | 626 | 59 (44–70) |
| Global patient VAS, median (IQR) | 622 | 65 (50–78) |
| Global doctor VAS, median (IQR) | 598 | 60 (45–70) |
| DAS28, median (IQR) | 604 | 5.82 (5.17–6.56) |
| ESR (mm/1st h), median (IQR) | 618 | 28 (15–44) |
| CRP, median (IQR), mg/l | 614 | 20 (8–39) |
| Haemoglobin, median (IQR), g/dl | 626 | 12.4 (11.5–13.4) |
| Seropositivity for RF,% | 551 | 473 (86) |
| Anti-filaggrin antibody, *n* (%) | 501 | 187 (37) |
| Antinuclear antibody, *n* (%) | 350 | 285 (50) |
| Tenosynovitis, *n* (%) | 635 | 228 (36) |
| Rheumatoid nodules, *n* (%) | 635 | 139 (22) |
| Radiographic erosions, *n* (%) | 589 | 514 (87) |
| Narrowing joint, *n* (%) | 589 | 512 (87) |
| Treatments already prescribed, *n* (%) | | |
| NSAID, *n* (%) | 625 | 584 (93.4) |
| Corticosteroid, *n* (%) | 622 | 586 (94.2) |
| Hydroxychloroquine, *n* (%) | 618 | 382 (61.8) |
| Gold salts, *n* (%) | 620 | 356 (57.4) |
| Penicillamine, *n* (%) | 602 | 141 (23.4) |
| Sulfasalazine, *n* (%) | 611 | 316 (51.7) |
| MTX, *n* (%) | 629 | 621 (98.7) |
| Azathioprine, *n* (%) | 591 | 49 (8.3) |
| Cyclosporin, *n* (%) | 595 | 78 (13.1) |
| Leflunomide, *n* (%) | 614 | 337 (54.8) |

IQR: interquartile range.

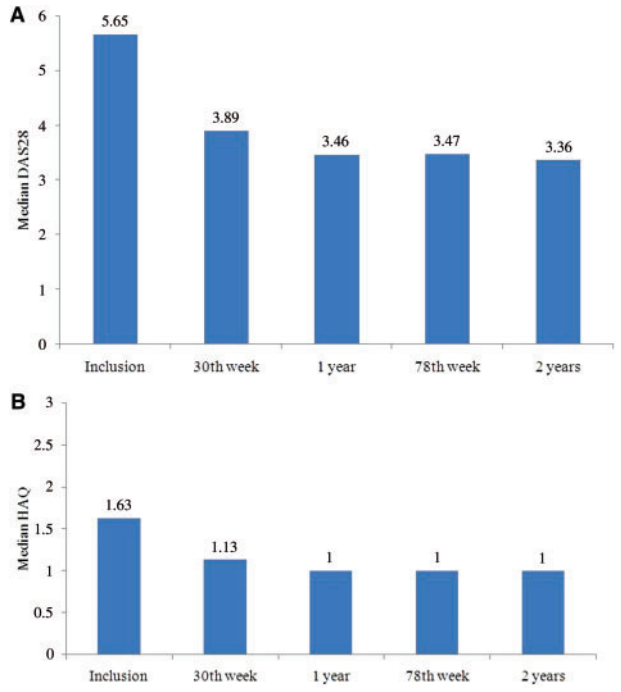


FIG. 1. Evolution of (**A**) the median DAS28 score and (**B**) the HAQ score.

At the beginning, almost all of the patients responded with only 16 (3%) interruptions for inefficacy. After the first four perfusions, the greatest number of drop-outs due to inefficacy was observed in 50 (9%) patients; during the past 50 weeks, the interruption was possible at all times, in 43 (11%) patients.

Of the 635 patients receiving at least one perfusion, 2002 adverse effects were reported in 522 (82%) of them. The main adverse effects consisted of infection (51% of the adverse effects) of bacterial (68% of the infections including one tuberculosis and three septicaemias), viral (50%), herpes (7%), fungal (7%) and parasitic (0.6%, one strongyliasis and one taenia) origin. No cases of lymphoma were detected. Five deaths were noted of which two were attributed to infliximab (one miliary tuberculosis and one septicaemia).

Among the 403 and 244 patients treated, respectively, for 1 year and during the entire study, 18% (73) and 21% (52), respectively, presented at least one reaction to the perfusion. The mean number of reactions was 2.6 and 4.6, respectively, during the first and second years. The highest frequency (6%) was observed as of the first perfusion and tended to decrease, very slightly over time. During the first and second years of the study, respectively, 188 (4%) and 238 (3.7%) reactions were noted for 4676 and 6448 perfusions. This reaction was therefore independent of the duration of the treatment.

The initial mean dose of infliximab administered was 3.16 mg/kg, then increased, after first (374 patients) and second years (244 patients), to 3.44 mg/kg (+9%) and 3.56 mg/kg (+13% with respect to the initial dose), respectively. The 403 and 244 patients treated, respectively, during the first and second years received an average of 8.9 and 14.7 perfusions, respectively.

### *Medico-economic results*

Among the 403 (63.5%) and 244 (38.4%) patients still monitored over the first and second years, 355 (88%) and 163 (67%), respectively, completed all of the medico-economic questionnaires. The average cumulative annual cost was €27 665 per patient after the first year, of which 88.4, 10.4 and 1.2% was due to the direct medical (essentially hospitalization, infliximab), indirect (loss of production) and direct non-medical (transport) costs, respectively. Infliximab accounted for €21 232 (drug, preliminary lab tests and hospitalization for perfusion) in the first year or 76.7% of the total costs. After 2 years, the cumulative cost represented €47 295 per patient with a similar distribution of the different costs. Before the use of infliximab, the mean annual cost for the treatment of RA was €9831. During the first year, excluding the cost of infliximab, it decreased to €6433 (–34.6%, $P < 0.01$) due to the reduction in direct medical (−22.5%), indirect (−32.1%) and direct non-medical (−77.3%) costs. The detailed examination of the direct medical costs (excluding infliximab) revealed a decrease in all of the components ($P < 0.01$) (hospitalization, drugs, surgery, etc.) except for the physiotherapy (multiplied by over five during the first year). The cost was analysed according to the HAQ (HAQ $\leqslant 1$, $1 < \text{HAQ} \leqslant 1.5$, $1.5 < \text{HAQ} \leqslant 3$) upon inclusion (Table 3). After the first year, a significant difference was noted between the levels of HAQ for the total costs ($P = 0.03$) as before the administration of infliximab ($P < 0.01$). The costs remained higher in patients with a major functional disability. After 2 years, the difference (including, in this case, the indirect costs) was not significant ($P = 0.07$), but the tendency was the same. The difference concerned the direct non-medical and indirect medical costs. The direct medical costs were significantly different the previous year according to the HAQ, but not after first and second years (Table 3).

When the effectiveness was expressed in clinically significant units (1 U equivalent to 0.25 HAQ points), the difference between the previous and first year under infliximab was significant, mean of 1.86 (95% CI 1.72, 2.00). For the HAQ $\leqslant 1$, $1 < \text{HAQ} \leqslant 1.5$ and HAQ > 1.5 groups at inclusion, the differences were 0.80 (95% CI 0.46, 1.14), 1.69 (95% CI 1.25, 2.12) and 2.24 (95% CI 1.85, 2.63), respectively. In the total sample, the INB($\lambda$) was significantly positive for $\lambda > 18\,593$. According to the HAQ, it was for $\lambda > 41\,821$, 14 721 and 9841, respectively (Fig. 2).

When the effectiveness was expressed in QALYs, using Barton's model (with a random effect), the mean difference of QALY was significant in whole sample (0.15; 95% CI 0.10, 0.20), in $1 < \text{HAQ} \leqslant 1.5$ and HAQ > 1.5 groups [0.14 (95% CI 0.06, 0.21) and 0.18 (95% CI 0.11, 0.25), respectively], but not

TABLE 3. Cost of treatment in euros by level of HAQ score

| | | Previous year | | | 1 year | | | 2 years | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | HAQ groups | Mean cost, € | Range | $P^a$ | Mean cost, € | Range | $P^a$ | Mean cost, € | Range | $P^a$ |
| Direct medical costs | All HAQ | 4175 | [0–78 011] | | 24 453 | [17 266–54 885] | | 41 375 | [28 647–87 181] | |
| | HAQ < 1 | 3093 | [91–21 508] | | 23 593 | [17 917–35 068] | | 40 453 | [28 647–79 946] | |
| | 1 < HAQ < 1.5 | 3689 | [0–25 487] | 0.009 | 23 502 | [17 266–40 023] | 0.12 | 39 907 | [29 307–61 430] | 0.33 |
| | HAQ > 1.5 | 4628 | [80–78 011] | | 25 125 | [17 346–54 885] | | 42 403 | [29 875–87 181] | |
| Direct non-medical costs | All HAQ | 1418 | [0–21 342] | | 322 | [0–3519] | | 626 | [0–8782] | |
| | HAQ < 1 | 554 | [0–3219] | | 181 | [0–1591] | | 368 | [0–2434] | |
| | 1 < HAQ < 1.5 | 893 | [0–4776] | <0.001 | 274 | [0–2531] | 0 | 497 | [0–3912] | 0.01 |
| | HAQ > 1.5 | 1834 | [0–21 342] | | 383 | [0–3519] | | 775 | [0–8782] | |
| Indirect costs | All HAQ | 4239 | [0–40 260] | | 2875 | [0–44 672] | | 5294 | [0–36 582] | |
| | HAQ < 1 | 2986 | [0–23 119] | | 2245 | [0–25 653] | | 3512 | [0–34 619] | |
| | 1 < HAQ < 1.5 | 4190 | [0–23 119] | 0.002 | 2800 | [0–23 424] | 0.04 | 5285 | [0–24 062] | 0.01 |
| | HAQ > 1.5 | 4554 | [0–40 260] | | 3083 | [0–44 672] | | 5893 | [0–36 582] | |
| Total costs | All HAQ | 9831 | [138–87 417] | | 27 650 | [17 957–76 237] | | 47 295 | [29 875–98 480] | |
| | HAQ < 1 | 6633 | [202–28 485] | | 26 020 | [17 986–57 007] | | 44 333 | [29 922–85 532] | |
| | 1 < HAQ < 1.5 | 8773 | [138–31 883] | <0.001 | 26 575 | [18 105–54 361] | 0.03 | 45 689 | [30 753–65 318] | 0.07 |
| | HAQ > 1.5 | 11 016 | [169–87 417] | | 28 591 | [17 957–76 237] | | 49 070 | [29 875–98 480] | |

[a]Comparisons using a Kruskal–Wallis test.

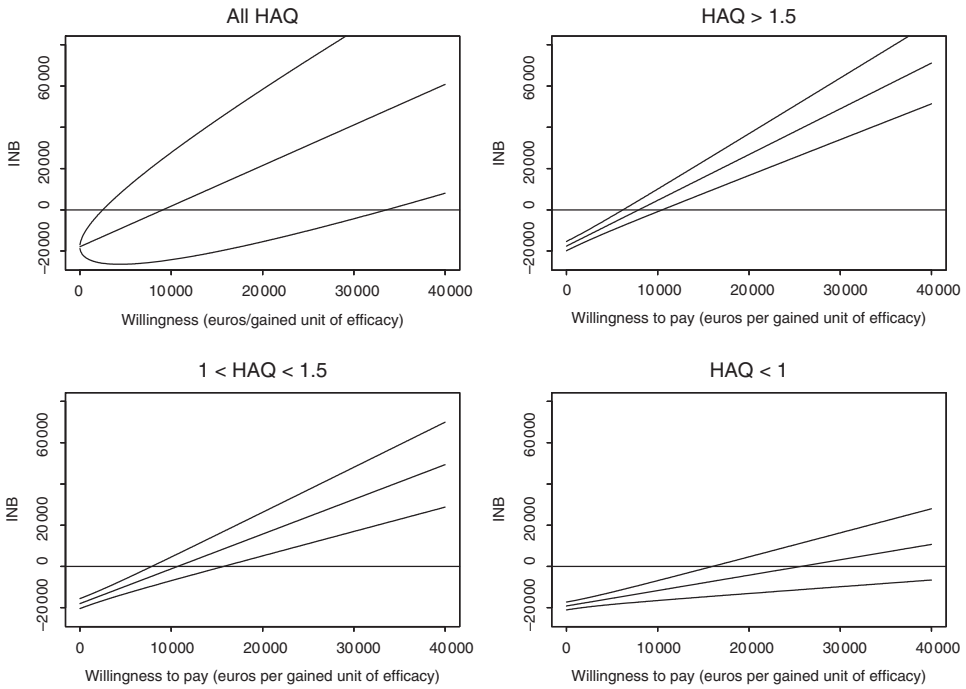


FIG. 2. INB (with 95% CI). The effectiveness was expressed in clinically significant units.

in the group HAQ < 1 (0.07; 95% CI 0.00, 0.13). The INB(λ) was, in the total sample, significantly positive for $\lambda > 249\,663$. In the HAQ ⩽1, 1 < HAQ ⩽1.5 and HAQ > 1.5 groups, it was significantly positive for $\lambda > 1\,107\,472$, 215 343 and 135 812, respectively. Using the BPM model, it was significantly positive for $\lambda > 371\,714$ in the total sample and, in the HAQ ⩽1, 1 < HAQ ⩽1.5 and HAQ >1.5 groups, for $\lambda > 836\,379$, 294 314 and 196 653, respectively.

## Discussion

The EMER study has confirmed the efficacy of infliximab in real life. A Swedish study [11] comparing cohorts treated by infliximab and etanercept, demonstrated an interruption in treatment after 2 years for half and one-quarter of the patients, respectively. An English study [12] based on registers demonstrated, after 6 months, the similar therapeutic maintenance under infliximab and etanercept for 79 and 80% of the patients, respectively. A Belgian study on 511 RA patients [13], demonstrated after 4 years, a maintenance under infliximab of 61.6%. In a Dutch study on 120 RA patients [14], 66% were still under infliximab after 1 year. In France, a therapeutic maintenance of 70% after 2 years was reported in 50 patients [15]. In our study, out of 635 patients, a therapeutic maintenance of 64% was noted after 1 year.

A retrospective American study [16] based on registers demonstrated, in 89 RA patients treated by infliximab, an average increase in the initial dose (3 mg/kg) of 33% after 24 months. Another study [17] in 141 patients demonstrated a 37.4% increase in dosage. After 2 years, our study demonstrated the same tendency with over one-quarter of the patients treated with >3 mg/kg. The efficacy in our study was similar to that of the ATTRACT study [3], in particular as regards the HAQ, as well as the profile of serious adverse effects and reactions to the perfusions.

As regards the economic data, a retrospective French study, comparing etanercept and infliximab in 58 patients [18],

demonstrated that the mean cost is similar, ~€19 500 per year, 70% (for infliximab) was attributed to the cost of the drug. A retrospective American study in patients aged >65 years [19] evaluated the annual cost under infliximab at ~$35 000, 50% was due to the cost of the drug. Our study found similar results with an average cost, in the first year, of €21 232 for infliximab, the total medical care of the patient amounting to €27 665.

Cost–effectiveness studies published on infliximab in RA patients were retrospective, comparative with a reference cohort and did not always include the indirect costs. Two analyses were carried out in parallel [20], in Great Britain and Sweden. The difference in clinical efficacy between infliximab and MTX in the ATTRACT study was used as a reference to which the epidemiological data and consumption of resources and the official rates for each country were applied. The ERAS study grouping 1473 RA patients for Great Britain and a cohort of 183 patients for Sweden, monitored for an average of 7.8 and 11.3 years, respectively, were considered. The costs and consequences of the progression of the RA were estimated with Markov's model. The difference in the results [20] between the two countries was most likely due to the higher indirect costs in Sweden in case of a progression of the disability. Thereby, when the RA was controlled, the price to pay for the monitoring was lower than that in Great Britain. An American study [21] also extrapolated the clinical results from the ATTRACT study on the ARAMIS cohort (4258 patients), representing a total of 17 085 patients/years. The cost of treatment was based on the fees relating to a perfusion (3 mg/kg) repeated 8 and 15 times, respectively, in the first and second year. The indirect costs were determined in the subgroup of patients employed upon inclusion. The analysis demonstrated that the association of infliximab–MTX (*vs* MTX alone) for first or second year increased the life expectancy expressed in QALYs. Modelization of the cost–efficacy ratio, carried out in Great Britain in the National Institute for Health and Clinical Excellence study [22], estimated the cost at £38 000/QALY for the use of infliximab in RA. In our study, it was only possible to enter the costs the previous year and for the 2 years of treatment. In these conditions, the annual cost of the medical treatment (infliximab–MTX association) represented the main cost. The similarity of the results, whatever the method used to express the effectiveness from the HAQ, provided us with the strength of the conclusion. The results in QALY demonstrated that for patients with an HAQ $\leqslant$1.5 and more specifically $\leqslant$1, the resources devoted to gain 1 U of effectiveness were much higher than for the other patients (HAQ > 1.5). In other words, the more severe the RA, the more cost-effective was infliximab. For these severe patients, the INB was significantly in favour of infliximab for values of willingness to pay >€135 812 and €193 653 according to the model, which was not acceptable in our society. A short follow-up can be a problem for cost-effective study in chronic disease.

Our study was of interest since it was carried out in real life, in a prospective manner, on a large number of patients without comparison with another cohort. The economic analysis did not demonstrate the cost–effectiveness using INB because the follow-up is very short. Part of the cost of infliximab was made up for by a reduction in hospitalizations as of the first year. The evaluation of the long-term costs was required in order to determine the full economic benefits of this treatment. In 2001, infliximab was the only anti-TNF-$\alpha$ agent available in France. As several biotherapy agents are now available to treat RA, it is probably inadequate to follow a cohort of patients for a long time on the same treatment. Medico-economic studies should be carried out taking the different therapeutic strategies into account (substitution, association) in clinical practice within a single cohort. Then the study period on a specific drug should remain short. This issue, when results are compared with a Markov model, has a conservative approach as a consequence (under evaluation of drug efficiency).

**Rheumatology key messages**

- The costs induced by biotherapies are important but difficult to measure.
- Our medico-economic analysis of infliximab in RA demonstrated gains in units of efficacy for patients but not in QALY on two years of follow-up.

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